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Mechanical and Water Vapor Transmission Properties of Polysaccharide Films

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ABSTRACT

The film-forming properties of chitosan, chitosan glutamate, sodium alginate, and hydroxypropyl methylcellulose (HPMC) were investigated. Films were produced by a casting/solvent evaporation method from plasticizer-free and plasticizer-containing aqueous solutions. The water vapor transmission and mechanical properties (puncture strength and % elongation) of the films were investigated as a function of the polymer type and viscosity, plasticizer type (glycerin, propylene glycol, polyethylene glycol, triethyl citrate), plasticizer concentration, and type and concentration of acid used to dissolve chitosan. The effect of storage humidity was also examined. Glycerin and water were good plasticizers for chitosan glutamate. The chitosan film properties were dependent on the type and concentration of acid used to dissolve it, citric acid being a good plasticizer. The mechanical and water vapor transmission properties of alginate and HPMC films were less influenced by the investigated variables.

INTRODUCTION

The problems associated with organic solvent based film coatings (cost, safety, and environmental pollution) and the advantages of aqueous-based systems have long been known. There is a tendency for industry to switch from organic coating to aqueous coating (1,2). The aqueous coating materials which are presently used for pharmaceutical products are predominantly either cellulose derivatives, mainly low-viscosity grades of hydroxypropyl methylcellulose (HPMC) (3–5), or acrylic resin derivatives (6).

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Recently, new water-soluble polymers have been introduced which may find an application in aqueous coating technology. Chitosan [β-(1-4)-2-amino-2-deoxy-D-glucose] is a cationic polyelectrolyte prepared by N-deacetylation of chitin, a principal component of shells of crustaceans and insects (7). Chitosan has been reported to be biodegradable, nontoxic, and biocompatible (8); it has a variety of promising pharmaceutical applications and is presently being investigated as a novel carrier material for different drug-delivery systems. Chitosan is a good excipient for directly compressed tablets and a vehicle for either improving the dissolution rate and bioavailability of poorly water-soluble drugs or for sustaining the release of water-soluble drugs (9). It is very promising as a coating material in microencapsulation processes (10–13).

Alginates are salts of aginic acid, which is a linear copolymer composed to 1,4-linked β-D-mannuronic acid and α-L-guluronic acid residues, and are isolated from brown seaweeds (14). Alginates have been traditionally used in immobilizing living cells (15) and are currently investigated for controlled delivery of drugs or macromolecular active compounds, such as vaccines and peptides, specifically in microencapsulated forms (16–18).

Studies on pharmaceutical film coatings have often examined the permeability to water vapor as well as the ability to provide mechanical protection for solid dosage forms. These properties are generally examined on free films prepared by casting or spraying techniques (3,5,19). The mechanical properties are traditionally evaluated by stress-strain tensile tests (3,9). In reviewing the literature, rarely have the mechanical (20–23) and water vapor transmission properties (20) of chitosan-free films been investigated. In most of the studies, the films were produced from blends of chitosan and other polymers such as cellulose, polyvinyl alcohol, or polyvinyl pyrrolidone.

In this study, films of chitosan, chitosan glutamate, sodium alginate, and hydroxypropyl methylcellulose (HPMC) were prepared by a casting/solvent evaporation process, and characterized by measuring their mechanical behavior using a puncture test and their water vapor transmission properties. The effects of the type and molecular weight of polymer, type and concentration of plasticizer, type and concentration of acid used to dissolve chitosan, and storage humidity on the film properties were evaluated.

MATERIALS AND METHODS

Materials

The following chemicals were obtained from commercial suppliers and used as received:

Chitosan glutamate (supplier's specification: viscosities of 1% w/w aqueous solutions at 25°C were <20 and 20–200 cps for Sea cure +110 and +210), Protan Lab., Drammer, Norway.

Chitosan (supplier's specification: viscosities of 1% w/w aqueous solutions in 1% v/v acetic acid at 25°C were <20 and 20–200 cps and degree of deacetylation was >80 for Sea cure 123 and 223), Protan Lab., Raymond, WA.

Sodium alginate (supplier's specification: viscosities of 2% aqueous solutions at 25°C were 250 and 3500 cps), Sigma Chemical Co., St. Louis, MO.

Hydroxypropyl methylcellulose (HPMC) (supplier's specification: viscosities of 2% aqueous solutions at 20°C were 3, 5, 15, and 50 cps for Methocel E3, E5, E15LV, E50 Premium Grade), Dow Chemical Co., Midland, MI.

Glycerin (certified ACS), propylene glycol (PG) (USP/FCC), and citric acid monohydrate, Fisher Scientific Co., Fair Lawn, NY.

Polyethylene glycol 400 (PEG), Spectrum Chemical Mfg. Corp., Gardena, CA.

Triethyl citrate (TEC), Morflex Chemical Co., Greensboro, NC.

Acetic, lactic, and propionic acid, Mallinckrodt Specialty Chemicals Co., Paris, KY.

Water was double-distilled.

Methods

The polymeric films were produced by a casting/solvent evaporation technique. Unplasticized and plasticized polymer solutions (5% w/w) were prepared by dissolving chitosan glutamate, sodium alginate, and HPMC in double-distilled water and chitosan in a diluted acidic (1 M) solution at room temperature. The solutions were sonicated, left to stand until removal of trapped air bubbles, and poured on a Teflon protective overlay (Cole-Parmer Instrument Co., Chicago, IL,) mounted on a glass plate. The films were air dried for 48 hr at room temperature and then oven dried for 24 hr at 40°C [area of casting = 18 × 10 cm^2; standard formulation: casting weight = 73 g; total solids content = 3.65 g; plasticizer content based on polymer = 30% w/w; mixing time with plasticizer = 4 hr; approximate dry film thickness = 164 μm (chitosan glutamate), 203 μm (chitosan acetate); 142 μm (sodium alginate), and 183 μm (HPMC)]. The dried films were cut into 4 × 4 cm^2 test sections and stored at room temperature at 54% relative humidity for 48 hr. The thickness of the dry films was determined in five places with a micrometer (P. N. Gardner Co., Inc., Pompano Beach, FL).

To determine the mechanical properties of dry films, a puncture test was performed on an Instron (Model 4201, Instron Corp., Canton, MA). A puncturing probe, which was attached to the cell of an Instron, was driven downward through the polymeric film (4 × 4 cm^2 test sections) placed within the holding device. The experimental details and the conversion of the load (kilograms) and displacement (millimeters) at film rupture to puncture strength (megapascals) and % elongation were previously described (6). The conversion of peak load to puncture strength provided the normalization of the data for the differences in film thickness. Each experiment was repeated at least 4 times.

To measure the water vapor transmission, disks were punched from the polymeric films, placed on open 4-ml glass vials containing 2 g of a desiccant (silica gel), and held in place with a screw lid with an opening of 8 mm (test area: 0.50 cm^2). The vials were conditioned in a desiccator containing silica gel for 12 hr. The vials were then placed in desiccators containing saturated salt solutions to give relative humidities of 33%, 54%, 75%, and 100% (24). The moisture transmitted through the polymeric films was determined gravimetrically by weighing the vials initially and over a 72-hr period (2, 8, 12, 24, 48, and 72 hr, $n = 3$). The rate of water vapor transmission was obtained from the slope of the line resulting from water vapor transmitted versus time plots. A control vial (containing only silica gel) was also introduced into the desiccators.

The following variables were investigated: type and molecular weight of polymer (films containing 30% w/w glycerin; for chitosan glutamate: Sea cure +110 and +210; chitosan: Sea cure 123 and 223; sodium alginate: 250 cps and 3500 cps; HPMC: Methocel E3, E5, E15LV, E50); concentration of plasticizer (glycerin; 5%, 10%, 15%, 20%, 25%, and 30% w/w based on polymer, for Sea cure +110, Sea cure 223/acetic acid, sodium alginate 250 cps and Methocel E50); type of plasticizer (glycerin, PG, PEG and TEC; 30% w/w based on polymer, for Sea cure +110, sodium alginate 250 cps and Methocel E50); type of acid for chitosan films (acetic acid, citric acid, lactic acid, propionic acid; acid concentration = 1 M; for Sea cure 223); concentration of acid used to dissolve chitosan (acetic acid: 0.5, 1.0, 1.5, and 2.0 M; citric acid: 0.50, 0.75, 1.00, and 1.25 M; for Sea cure 223); and storage humidity. The films were conditioned in desiccators containing silica gel or different saturated salt solutions to give relative humidities of 0%, 33%, 54%, and 75%, respectively, at 22°C (24) (unplasticized films, storage time = 2 days; films containing 30% w/w glycerin, storage time = 7 days; for Sea cure +110, sodium alginate 250 cps and Methocel E50).

RESULTS AND DISCUSSION

This paper discusses the effect of several variables on the mechanical and permeability properties of polysaccharide films. The polymeric films were prepared by casting and drying plasticized and nonplasticized aqueous solutions of chitosan glutamate, chitosan, sodium alginate, or HPMC. All the films produced from the plasticizer-free solutions were smooth and transparent, but very brittle. Therefore, several plasticizers were added with the aim of improving their mechanical properties.

The plasticizer is the most important formulation factor affecting mechanical properties of films. It shifts the glass transition temperature to lower temperatures (25). In this study, the effect of the plasticizer concentration was investigated by adding increasing amounts of glycerin (5–30% w/w based on the polymer, with increments of 5% w/w) to chitosan glutamate, chitosan acetate, sodium alginate, and HPMC solutions (Fig. 1).

With all polymers, a glycerin level of 10% w/w was sufficient to obtain flexible films. The plasticizer-free films or films plasticized with 5% w/w glycerin absorbed water and became more flexible after conditioning at 54% relative humidity for 2 days. The addition of larger amounts of glycerin to chitosan glutamate resulted in significant changes in the mechanical properties, making the polymer softer and more flexible. The elongation (E) increased and the puncture strength (PS) decreased with increasing glycerin concentration. Films containing 30% w/w glycerin were very soft and weak due to excessive amounts of plasticizer; films with 10–20% w/w glycerin had suitable toughness and flexibility as a film-coating material (3). As a result of the decreasing puncture strength and increasing elongation, the modulus at break (calculated from the ratio of puncture strength to % elongation; data not shown) of chitosan glutamate films decreased with increasing glycerin concentration (modulus at break of plasticizer-free films: 8 MPa; modulus at break of films plasticized with 10% w/w glycerin: <1 MPa). These results revealed that glycerin is an efficient plasticizer for chitosan glutamate. HPMC films were also effectively plasticized by glycerin (% elongation increased from 9 to 37 after addition of 30% w/w glycerin while the puncture strength remained nearly constant). Chitosan acetate and sodium alginate films were less plasticized by glycerin at the investigated concentrations, as shown by small changes in puncture strength and % elongation.

As expected (5), the mechanical properties were found to be dependent on the polymer type and molecu-

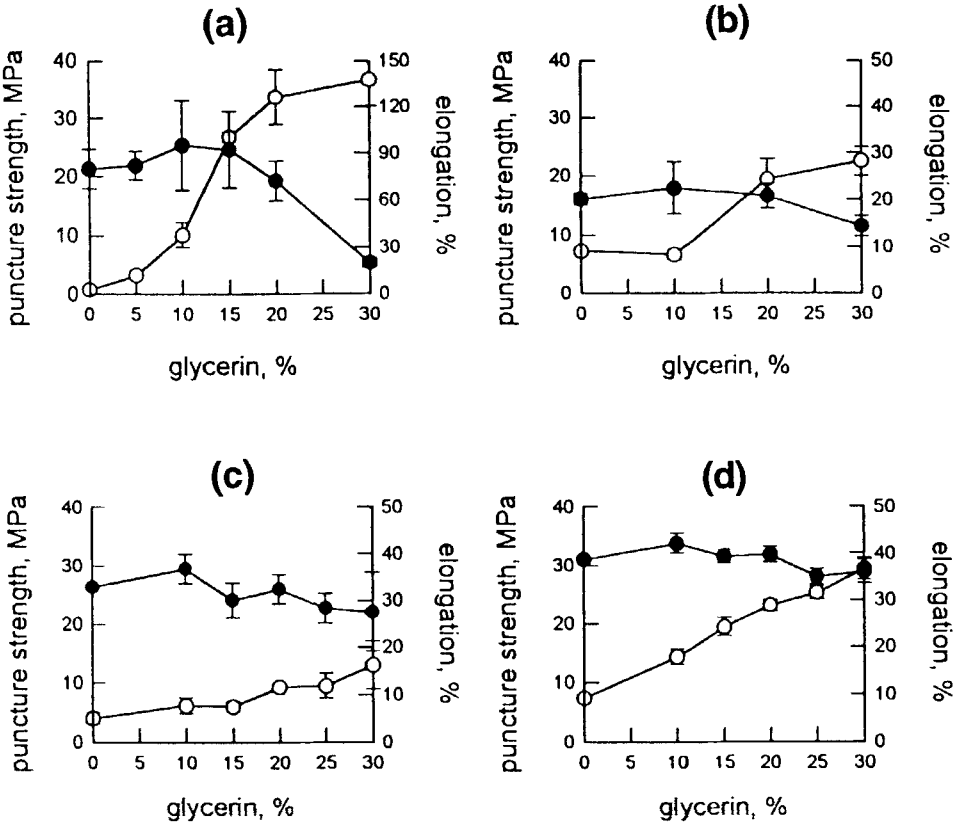

Figure 1. Effect of glycerin concentration on the puncture strength and % elongation of (a) chitosan glutamate, (b) chitosan acetate; (c) sodium alginate, and (d) HPMC films: ●, puncture strength; ○, % elongation.

lar weight (see Table 1). The flexibility of the films increased with increasing molecular weight (MW).

It is well known that the extent of the change in the glass transition temperature is dependent upon the type of plasticizer and the polymer (26–28). Thus, different plasticizers, at the same concentration level, will affect the glass transition temperature and hence the mechanical properties to a different extent. A series of plasticiz-

Table 1

Effect of Polymer Type and Molecular Weight on the Mechanical Properties of Various Polysaccharide Films (Solids Content = 5% w/w; Glycerin Content = 30% w/w Based on Polymer; SD in Parentheses)

	Chitosan Glutamate[a] Sea Cure		Chitosan[b] Sea Cure		Sodium Alginate[a] Viscosity (cps)		HPMC			
	+110	+210	123	223	250	3500	E3	E5	E15LV	E50
Thickness (μm)	164	146	117	103	142	129	190	189	161	183
	(9)	(10)	(13)	(9)	(5)	(1)	(15)	(12)	(13)	(12)
PS (MPA)	5.42	2.57	7.67	18.01	21.99	31.97	1.68	6.44	16.49	28.90
	(0.98)	(0.69)	(1.41)	(3.10)	(6.71)	(2.04)	(0.38)	(0.52)	(3.36)	(2.08)
E (%)	132.36	173.37	19.88	62.73	16.18	29.93	1.66	10.48	20.34	36.73
	(18.97)	(30.85)	(2.86)	(8.74)	(5.02)	(8.28)	(0.44)	(1.48)	(5.26)	(2.39)

[a]Cast from 5% w/w aqueous solution.
[b]Cast from 2.5% w/w solutions in 1 M acetic acid.

ers (glycerin, PG, PEG, and TEC) were compared for their effect on the mechanical properties of polysaccharides (see Table 2). The concentration of the plasticizer and total solids content were kept constant (plasticizer = 30% w/w based on the polymer, total solids content = 5% w/w). In addition to glycerin, PG proved to effectively plasticize chitosan glutamate; large changes in the mechanical properties were produced. The TEC and PEG were, however, less effective. To be effective, the liquid plasticizer must blend uniformly and homogeneously with the polymer and remain blended when cooled to room temperature. Unplasticized chitosan glutamate films and films plasticized with 30% glycerin or PG were transparent while films plasticized with 30% PEG or TEC were brittle and opaque. This might be attributed to the incompatibility between plasticizer and polymer, as was confirmed by scanning electronic microscopy. The surface of the unplasticized films or films plasticized with 30% glycerin and PG appeared very smooth while those plasticized with 30% PEG and TEC showed a porous surface due to plasticizer leaching.

HPMC films containing 30% glycerin, PG, or PEG were clear and flexible, while HPMC films containing 30% TEC were opaque. This might be related to some polymer-plasticizer incompatibility. However, they were flexible; the puncture strength decreased from 31 to 4 MPa and elongation increased from 9 to 42% after addition of 30% TEC. The most suitable plasticizer for sodium alginate was glycerin; plastification with 30% w/w PEG or TEC resulted in opaque and brittle films.

In addition to the polymer and type and concentration of plasticizer, the mechanical properties were considerably influenced by the storage conditions. All nonplasticized films, which were initially brittle, absorbed moisture from the air and became very flexible after standing at ambient conditions. The effect of water as a plasticizer was demonstrated by conditioning the nonplasticized films in desiccators of 33%, 54%, 75%, and 100% relative humidity for 2 days (see Fig. 2). The storage at a high humidity produced an effect similar to that of plasticizers on the mechanical behavior. Pronounced changes occurred in puncture strength and % elongation; the puncture strength decreased and the % elongation increased with increasing storage humidity with all polymers. Chitosan glutamate films which were conditioned at 33% relative humidity were very brittle and weak, as shown by low values of both puncture strength and elongation; they broke into small pieces during the puncture test. The same films conditioned at 75% or 100% relative humidity were flexible and had a circular hole after puncturing.

Films containing 30% w/w glycerin were stored at 0%, 33%, 54%, and 75% relative humidity for 7 days (Fig. 3). The % elongation of chitosan glutamate films greatly increased with increasing humidity; again sodium alginate and HPMC were nearly unaffected by humidities below 54%. These findings can be related to the moisture uptake data. Chitosan and alginate films lost approximately 5% moisture, as expressed in weight percentage, when stored at 0% relative humidity and

Table 2

Effect of Type of Plasticizer on the Puncture Strength and % Elongation of Polymeric Films (Solids Content = 5% w/w; Plasticizer Content = 30% w/w Based on Polymer; SD in Parentheses)

	Chitosan Glutamate, Sea Cure +110			Sodium Alginate, 250 cps			HPMC, Methocel E50		
Plasticizer	Thickness (μm)	PS (MPa)	% E	Thickness (μm)	PS (MPa)	% E	Thickness (μm)	PS (MPa)	% E
None	178	21.37	2.59	194	26.34	5.03	206	30.97	9.25
	(13)	(3.39)	(0.43)	(21)	(3.69)	(1.29)	(13)	(0.00)	(0.67)
Glycerin	164	5.42	137.62	142	22.01	16.18	183	28.90	36.73
	(9)	(0.98)	(11.15)	(5)	(6.71)	(0.10)	(12)	(2.08)	(2.39)
PG	145	7.03	100.35	154	36.78	13.90	152	34.74	17.58
	(5)	(1.21)	(9.46)	(32)	(2.09)	(1.82)	(14)	(2.69)	(1.02)
PEG	175	12.28	4.38	282	6.84	4.18	175	27.33	22.83
	(12)	(1.65)	(0.45)	(20)	(0.29)	(0.24)	(11)	(2.63)	(1.77)
TEC	159	7.95	1.38	161	21.84	6.00	176	3.58	42.44
	(21)	(2.16)	(0.37)	(11)	(1.22)	(0.46)	(11)	(1.38)	(1.07)

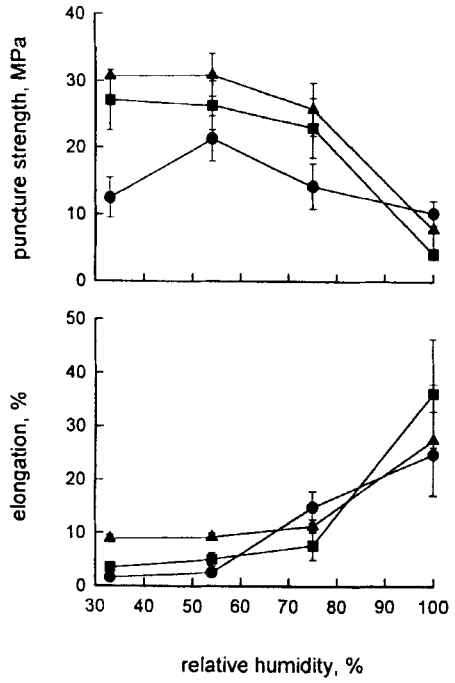

Figure 2. Effect of relative humidity on the puncture strength and % elongation of unplasticized (●) chitosan glutamate, (■) sodium alginate, and (▲) HPMC films (temperature = 22°C; storage time = 2 days).

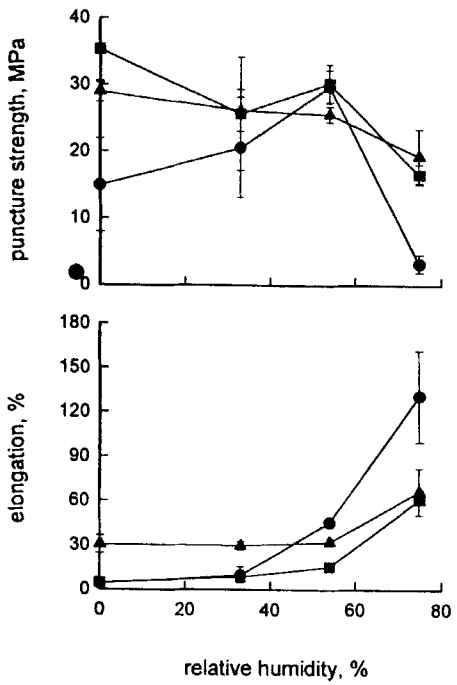

Figure 3. Effect of relative humidity on the puncture strength and % elongation of plasticized (●) chitosan glutamate, (■) sodium alginate, and (▲) HPMC films (glycerin concentration = 30% w/w; temperature = 22°C; storage time = 7 days).

became brittle; only chitosan glutamate films absorbed moisture (1.7%) at 33% relative humidity. The moisture uptake by chitosan glutamate films significantly increased at 54% relative humidity; the films became very weak at 75% relative humidity. According to the above results, water acted as a good plasticizer for chitosan glutamate, the plasticizing effects of glycerin and water being additive. Thus, the water uptake by the plasticized films was greater and the films became more flexible at all humidities when compared to unplasticized films. Chitosan glutamate films must be protected from moisture during their storage in order to keep their original mechanical properties. On the contrary, the mechanical properties of sodium alginate and HPMC films were less affected by humidity. Their moisture uptake was below 2.5% except after storage at 75% relative humidity.

According to the data in Fig. 1, films made of chitosan glutamate were significantly more flexible than those made of chitosan acetate at any investigated plasticizer content; thus they were better plasticized by glycerin. The films differed mainly in the type of acid used to dissolve chitosan and, thus, in the type of salt formed. The effect of the type of acid (acetic, citric, lactic, propionic) on the mechanical properties was investigated by keeping the solids content (5% w/w) and the acid concentration (1 M) constant (see Table 3). Acetic and propionic acid resulted in films that were thinner and tougher, but less flexible, when compared to those obtained from chitosan solutions prepared with lactic or citric acids. Chitosan citrate and chitosan lactate films had very low puncture strength and modulus at break (data not shown) and large % elongation values. The chitosan films also differed in appearance after puncturing; chitosan citrate films were very flexible and ruptured at high elongation values. The different behavior observed with different acids may be due to the different interaction between the chitosan and the acids in solution, and thus the different spatial configuration of the chitosan molecules during the film formation (29).

The effect of acid concentration was investigated with films cast from acetic acid and citric acid solutions. Chitosan acetate films were stored at 54% relative humidity, and chitosan citrate at 0% and 54% relative humidity for 2 days. The mechanical properties of the chitosan films were little affected by the concentration of acetic acid (Fig. 4); however, they were greatly in-

Table 3

Effect of Type of Acid on the Mechanical Properties of Nonplasticized Chitosan Films (Sea Cure 223; Solids Content = 5% w/w; SD in Parentheses)

Acid (1 M)	Thickness (μm)	PS (MPa)	E (%)
Acetic	257 (17)	16.07 (1.01)	9.06 (0.67)
Propionic	295 (23)	14.86 (1.91)	8.94 (2.09)
Citric	646 (27)	0.36 (0.04)	30.43 (7.08)
Lactic	453 (24)	1.68 (0.14)	59.54 (5.77)

fluenced by the citric acid concentration (Fig. 5). The puncture strength and modulus at break of chitosan citrate films decreased with increasing citric acid concentration at both humidities. The % elongation of films stored at 0% relative humidity rose with increasing citric acid concentration. On the contrary, the % elongation of films stored at 54% relative humidity decreased inversely to the citric acid concentration as the film absorbed a high amount of water and became weaker. Citric acid acted as a plasticizer for chitosan, an effect which has already been reported (30). Consequently, films with sufficient flexibility and strength can be prepared by using citric acid without other plasticizers being required. However, the films must be protected from moisture uptake.

The presence of plasticizers can also affect the permeability of polymeric films (31–34). The water vapor transmission rate was strongly dependent on the experimental humidity (data not shown); a humidity of 75% was used for all the water vapor transmission studies. The moisture permeation through the polymeric films was studied as a function of the plasticizer concentration (Fig. 6). The humidity transmitted through chitosan glutamate and HPMC films increased with increasing glycerin content. With chitosan glutamate, a linear relationship was found between the water vapor transmission and the glycerin concentration at the investigated plasticizer levels. In addition, with chitosan glutamate and HPMC films, the water vapor transmission results are well in accordance with those of % elongation for

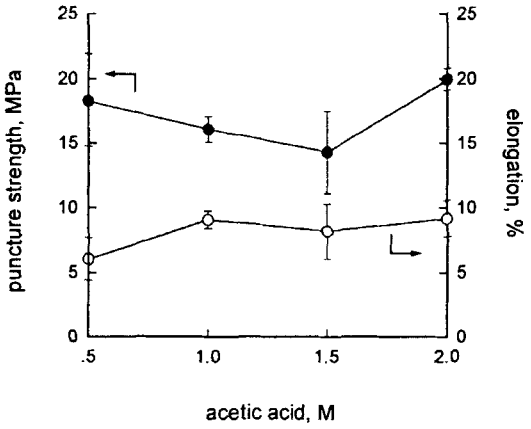

Figure 4. Effect of concentration of acetic acid on the puncture strength and % elongation of chitosan films.

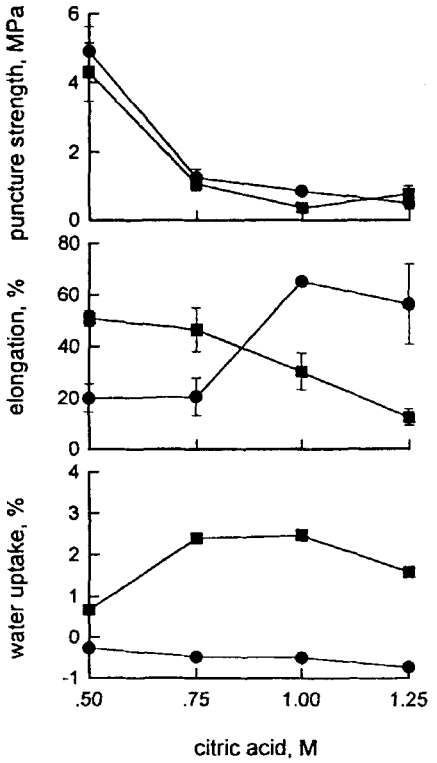

Figure 5. Effect of concentration of citric acid on the puncture strength and % elongation of chitosan films conditioned at (●) 0% and (■) 54% relative humidity (temperature = 22°C; storage time = 2 days).

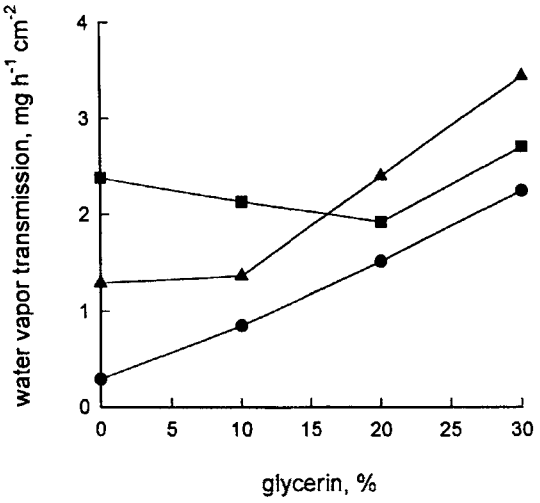

Figure 6. Effect of glycerin concentration on on the water vapor transmission through (●) chitosan glutamate, (■) sodium alginate, and (▲) HPMC films (glycerin concentration = 30% w/w).

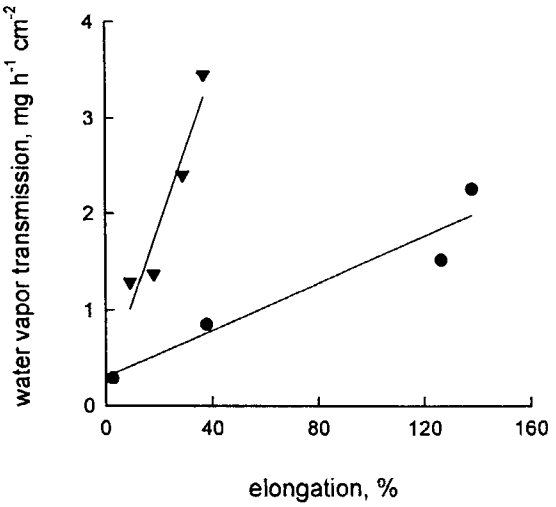

Figure 7. Relationship between the rate of water vapor transmission and % elongation for (●) chitosan glutamate and (▼) HPMC films.

Table 4

Effect of Polymer Type and Molecular Weight on Water Vapor Transmission of Various Polysaccharide Films (Glycerin Content = 30% w/w Based on Polymer, SD in Parentheses)

Chitosan Glutamate, Sea Cure		Sodium Alginate, Viscosity		HPMC Methocel		
+110	+210	250 cps	3500 cps	E3	E5	E50
1.90	2.22	1.74	1.92	2.37	2.49	2.43
Water vapor transmission rate (mg hr^{-1} cm^{-2})						

Water vapor transmission rate (mg hr^{-1} cm^{-2})

the same glycerin concentrations; linear relationships were found (Fig. 7). With sodium alginate, the moisture transmitted decreased with increasing glycerin concentration up to 20% w/w, followed by an increase. Plastification of chitosan glutamate with glycerin or PG increased the film permeability (nonplasticized films: 0.29 mg hr^{-1} cm^{-2}; films containing 30% glycerin: 1.90 mg hr^{-1} cm^{-2}; films containing 30% PG: 0.51 mg hr^{-1} cm^{-2}). On the contrary, PEG and TEC hardly affected the transmission through this polymer (data not shown).

As expected (5), the permeability of chitosan glutamate and sodium alginate films increased with increasing polymer molecular weight. The permeability of HPMC was, however, slightly dependent on the viscosity type (see Table 4).

In conclusion, the mechanical and water vapor transmission properties of chitosan glutamate films may be modified by relatively simple formulation changes. Glycerin and water are good plasticizers for chitosan glutamate, and citric acid, in addition of being a good solvent, is a good plasticizer for chitosan. The mechanical and water vapor transmission properties of alginate and HPMC films are less affected by the investigated variables.

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